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EXAMINER
GRUN, J

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/125,031

Applicant(s)
LONGACRE-ANDRE et al.

Examiner
James L. Grun, Ph.D.

Group Art Unit
1641



☒ Responsive to communication(s) filed on 22 Oct 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-45 is/are pending in the application.

Of the above, claim(s) 1-24 and 40-45 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 25-39 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

This Application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application clearly fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the sequences disclosed, e.g., on page 8.

Applicant is required to provide a substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, which includes each of the sequences disclosed in the specification as required by 37 CFR § 1.821(c). A substitute copy of the "Sequence Listing" in computer readable form must be provided as required by 37 CFR § 1.821(e). Applicant must also provide a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter as required by 37 CFR §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR § 1.821(g).

Applicant's election with traverse of Group I, claims 25-39 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the Examiner did not explain the "special" technical feature in each group and that the Patent and Trademark Office (PTO) has not applied the same standard as the International Preliminary Examination Authority (IPEA). These are not found persuasive because:

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the same standard was applied, i.e. PCT Rule 13, and the Examiner is not bound by the actions of the IPEA; and the technical feature shared between the claims as grouped is clearly set forth in the grouping of the claims, i.e. Group I shared the nucleic acid technical feature, Group II shared the antibody technical feature, and Group III shared the protein technical feature, as set forth these technical features define independent (i.e. not linked by a corresponding technical feature) and distinct structural products, and, in view of the IPER, as set forth, and now also in view of the rejections set forth infra, none of these technical features is considered special as claimed.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-24 and 40-45 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 7.

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed. When formal drawings are submitted, the draftsman will perform a review. Direct any inquiries concerning drawing review to the Drawing Review Branch at (703) 305-8404.

The disclosure is objected to because of the following informalities: the specification does not contain a separate section for and including the "Brief Description of the Drawings". Appropriate correction is required.

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The following is a quotation of the first paragraph of 35 U.S.C. § 112:

5 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

10 The specification is objected to and claim 39 is rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are: (1) known and readily available to the public; (2) reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809.

15 The specification lacks complete deposit information for the recombinant viruses deposited with the Collection Nationale de Cultures de Microorganismes (CNCM) as registration numbers I-1659, I-1660, I-1661, I-1662, and I-1663. Because it is not clear that biological materials possessing the properties of these viruses are known and publicly available or can be reproducibly isolated without undue experimentation, and because the invention of Claim 39 claims these specific deposited viruses, a suitable deposit for patent purposes is required. Without a publicly available deposit of the
20 above biological materials, one of skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the biological materials is an unpredictable event. A

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suitable deposit of the biological materials in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809 would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph.

5 If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty, that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the biological materials will be replaced should they ever become non-viable, would satisfy the deposit requirement made herein. Further, the specification should be amended to indicate the name and address of the depository.

10 If the deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR §§ 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

15 (a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

20 (d) the deposits were viable at the time of deposit; and,

(e) the deposits will be replaced if they should ever become non-viable.

Claims 25-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for every possible DNA or baculovirus construct, or host cell transfected therewith, encoding an immunogenic fragment of the p19 fragment of the *Plasmodium*

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MSP-1 protein or an immunological equivalent. Applicant provides guidance only to the constructs as found in the deposited viruses given CNCM registration numbers I-1659, I-1660, I-1661, I-1662, and I-1663. Numerous changes can be made to a nucleotide sequence having over 290 residues and Applicant provides no guidance as to what changes can be made to the encoding nucleic acids which result in an “immunological response equivalent” of the encoded protein other than those changes in the nucleic acid codons which do not affect the encoded amino acid sequence of the protein/fragment as it is found in nature. Even single changes in the encoded amino acid sequence of a protein can have significant unpredictable effects upon the immunological response of that encoded protein. For example, the change of a single glutamine residue to glutamic acid was shown to affect antibody reactivities to a fragment of the p19 fragment of the *Plasmodium* MSP-1 protein (Chappel et al., Mol. Biochem. Parasitol. 60:303, 1993), i.e. the two allelic variants tested were not immunological equivalents. Random unpredictable experimentation, unguided by Applicant’s disclosure, would seem to be required to determine which changes function and which do not in the invention. Such random unguided experimentation is undue experimentation. Note that an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all possible analogs where the characteristics of the analogs are unpredictable. See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. (18 USPQ 2d 1027 (CAFC 1991)). The disclosure of an invention, wherein further unguided unpredictable experimentation by another is required to discover that which Applicant purports to be the invention, is not seen as providing an enabling disclosure. Moreover one would not know,

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absent further guidance from Applicant, what is encompassed by or how to use a baculovirus type vector other than baculovirus or a *Plasmodium* type parasite other than a *Plasmodium* species.

Further, constructs as instantly claimed appear to require nucleic acids encoding the N-terminal signal sequence of the MSP-1 protein for expression by recombinant baculovirus in Sf9 cells (Longacre et al., Mol. Biochem. Parasitol. 64:191, 1994; see page 201, column 2). The function of no signal sequence other than that of the MSP-1 protein is taught by Applicant in the invention and the ability of another signal sequence to result in appropriate expression of the protein would seem unknown and unpredictable. Thus, one would have no assurance of the ability to make and use constructs which function in the invention in the absence of these required sequences. The disclosure is not enabling for an invention of the scope as instantly claimed wherein those sequences critical or essential to the practice of the invention are not included in the claims. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

For the reasons set forth, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 25-39 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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In claim 25 and claims dependent thereupon, "baculovirus type modified vector" or "*Plasmodium* type parasite" are vague and indefinite with regard to the metes and bounds of the invention for which protection is desired because it is not clear what is encompassed by "type". In these claims, "the peptide sequence", "the surface protein 1", "the parasite surface", "the end of its penetration phase", "the expression product", "the corresponding parasite", "the range", and "the totality of nucleotides" lack antecedent basis. It is not clear what is encompassed by an "equivalent" immunological response. It is entirely unclear which of the previously recited first or second nucleotide sequences is the said nucleotide sequence, and it is entirely unclear what range of G and C content of the nucleotide sequence is encompassed by the claim as both broad (at least 50%) and narrow (40% to 60%) ranges of overlapping concentrations are recited.

In claim 26 and claims dependent thereupon, "said second polypeptide sequence" lacks antecedent basis as nucleotide sequences are recited in claim 25.

In claims 26-30, "A modified vector" should be --The modified vector--.

In claim 29 and claims dependent thereupon, "the hydrophobic C-terminal end sequence", "said recombinant protein", "the cell membrane", and "the host" lack antecedent basis. Moreover, it is not clear what sequence is encompassed by "the hydrophobic C-terminal end sequence" as the metes and bounds of the sequence are not clear and it is not clear how a nucleotide sequence has a hydrophobic C-terminal end sequence which can be deprived. Moreover, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and

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bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" or "in particular" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 29 recites the broad recitation "host", and the claim also recites "in particular in a cell of an insect infectable" which is the narrower statement of the range/limitation.

In claim 31 and claims dependent thereupon, "Sf9 type insect cell" is vague and indefinite with regard to the metes and bounds of the invention for which protection is desired because it is not clear what is encompassed by "type". Moreover, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. In the present instance, claim 31 recites the broad recitation "organism", and the claim also recites "in particular an Sf9 type insect cell" which is the narrower statement of the range/limitation.

In claim 32 and claims dependent thereupon, "the peptide sequence", "the surface protein 1", "the merozoite form", "the parasite surface", "the end of its penetration phase", "the expression

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product”, “the corresponding parasite”, “the range”, and “the totality of nucleotides” lack antecedent basis. It is not clear what is encompassed by an “equivalent” immunological response. It is entirely unclear what range of G and C content of the nucleotide sequence is encompassed by the claim as both broad (at least 50%) and narrow (40% to 60%) ranges of overlapping concentrations are recited.

5 In claims 33-38, “A synthetic DNA sequence” should be --The synthetic DNA sequence--.

In claim 33 and claims dependent thereupon, “the sequence coding for the hydrophobic C-terminal end region” lacks antecedent basis and is entirely unclear as to what sequence is encompassed. In these claims, “the p19 protein”, “the cell membrane”, and “the host” also lack antecedent basis. Moreover, a broad range or limitation together with a narrow range or limitation
10 that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. In the present instance, claim 33 recites the broad recitation “host”, and the claim also recites “in particular in a cell of an insect infectable” which is the narrower statement of the range/limitation.

In claim 34 and claims dependent thereupon, “the principal sequence” lacks antecedent basis
15 and thus it is unclear to what the signal nucleotide sequence is homologous or heterologous.

In claim 36 and claims dependent thereupon, “the expressed recombinant protein”, “the surface of the membrane”, “the host cell”, and “the principal nucleotide sequence” lack antecedent basis. Moreover, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting
20 claim does not clearly set forth the metes and bounds of the patent protection desired. In the present

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instance, claim 36 recites the broad recitation “3' sequence...heterologous”, and the claim also recites “in particular that from *P. vivax*” which is the narrower statement of the range/limitation.

In claim 38, “said 3'-terminal sequence” lacks antecedent basis at least in claims 32 and 34.

5 In claim 39, “baculovirus type vector” is vague and indefinite with regard to the metes and bounds of the invention for which protection is desired because it is not clear what is encompassed by “type”. The recitations of “the virus” lack antecedent basis. In this claim, improper Markush language is used to claim the members of the group. The alternatives “selected from...or” or “selected from the group consisting of...and” are acceptable.

10 Claims 26, 28-31, and 36-38 are objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

15 (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 25-39 are rejected under 35 U.S.C. § 102(b) as being anticipated by Longacre et al (Mol. Biochem. Parasitol. 64:191, 1994) in light of the instant disclosure.

Longacre et al teach recombinant baculovirus constructs comprising nucleic acid sequences encoding N-terminal amino acids of the *Plasmodium vivax* MSP-1 protein, either anchored or
5 secreted forms of both the C-terminal p42 fragment (which comprises the C-terminal p19 fragment) and the C-terminal p19 fragment of the *Plasmodium vivax* MSP-1 protein, and two TAA stop codons, all under the control of the polyhedrin promotor. In light of the instant disclosure (e.g. page 11) the constructs comprise nucleic acids with “relatively much higher amounts of G and C nucleotides than those of...*P. falciparum*”, and, absent evidence to the contrary, are inherently within
10 the recited ranges. With regard to claims 32-38, the peptides of the reference are considered as inherently capable of inducing an equivalent immunological response to the corresponding parasite (i.e. to *Plasmodium vivax*). Absent evidence to the contrary, and in light of Applicant’s disclosure (e.g. pages 5-6 and 33), the virus constructs of the reference are presumed by the Examiner to be those deposited viruses given CNCM registration numbers I-1659 and I-1660.

15 The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the
20 invention was made.

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(c) Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

5 This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

10 Claims 25-39 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Chappel et al (Mol. Biochem. Parasitol. 60:303, 1993), Miller et al (Mol. Biochem. Parasitol. 59:1, 1993), and Longacre et al (Mol. Biochem. Parasitol. 64:191, 1994).

 Chappel et al teach a recombinant baculovirus, similar in construction to that as instantly disclosed, i.e. having the amino terminal 34 amino acids of the *P. falciparum* MSP-1 protein fused
15 to 271 amino acid residues of the p42 fragment of the protein ending at residue 1723 of the sequence as disclosed and numbered in Miller et al (see page 6), which produces a soluble protein (because it lacks the putative glycosylphosphatidylinositol addition region C-terminal to the second EGF-like domain) and which includes both EGF-like domain structures of the p19 fragment of the MSP-1 protein. The reference teaches that the first EGF-like domain of the p19 fragment, by itself, contains
20 many of conformational epitopes recognized by known antibodies which bind to both the p42 and p19 fragments and inhibit parasite growth. In contrast to the invention as instantly claimed, the encoding nucleotides as found in nature in *P. falciparum* and used in the construct of the reference appear to not have a G and C content in the ranges of 40-60% or at least 50%.

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The teachings of Longacre et al are as set forth above. The reference admits that the construction of recombinant baculovirus comprising *Plasmodium vivax* MSP-1 protein fragments was guided by the previous functional constructs expressing the *P. falciparum* MSP-1 protein fragments. The reference demonstrates that baculovirus constructs containing an appropriate MSP-1 signal
5 sequence can be used for the expression of various length soluble or anchored C-terminal fragments of the MSP-1 protein.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have constructed a recombinant baculovirus expressing at least the first EGF-like domain of the C-terminal p19 fragment of the *P. falciparum* MSP-1 protein using any of the genus
10 of nucleotide sequences encoding the relevant amino acid sequence (Chappel et al in view of Miller et al) with well known methods, as in Chappel et al and Longacre et al, with an extremely reasonable expectation of success that the encoded sequence would be expressed by insect cells containing the baculovirus constructs in view of the successful production of a variety of like soluble and/or anchored MSP-1 fragments as taught in Chappel et al or Longacre et al. The substitution of *P. vivax*
15 signal and anchoring encoding sequences known to function for expression of the fragments of the protein in insect cells for the homologous sequences encoded by *P. falciparum* is well within the skill of an ordinary practitioner in the art and would not have been expected to influence the immunological function of the *P. falciparum* encoded and expressed p19 fragment in view of the teachings of Chappel et al that the first EGF-like domain of the C-terminal p19 fragment of the *P.*

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falciparum MSP-1 protein, by itself, contains many of conformational epitopes recognized by known antibodies which bind to both the p42 and p19 fragments and inhibit parasite growth.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

5 The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

10 A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

15 Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

 Claims 25-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 53-63 of copending Application No. 20 09/134,333. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims encompass overlapping genera which include the same baculovirus vectors and DNA.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 25-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-33 of copending Application No. 09/125,032. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of copending Application No. 09/125,032 claim baculovirus vectors and DNA which have encoding sequences which fully encompass those as claimed in the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Chang et al disclose baculovirus constructs comprising nucleic acid sequences encoding the C-terminal p42 fragment of the *Plasmodium falciparum* MSP-1 protein.


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Any inquiry concerning this communication or earlier communications from the Examiner should be directed to James L. Grun, Ph.D., Technology Center 1600, Group 1640, Art Unit 1641, whose telephone number is (703) 308-3980. The Examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

- 5 If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James C. Housel, SPE, can be reached on (703) 308-4027. The fax phone numbers for official communications to Group 1640 are (703) 305-3014 or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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James L. Grun, Ph.D.
January 28, 2000



CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641